

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte MARTIN C. WOODLE, IRMA A.J.M. BAKKER-WOUDENBERG,
and FRANCIS J. MARTIN

Appeal No. 95-4004
Application 07/858,171¹

ON BRIEF

Before WINTERS, SCHAFFER, and GRON, Administrative Patent Judges.

¹ Application for patent filed March 27, 1992. According to applicants, this application is a continuation-in-part of Application 07/642,231, filed January 16, 1991; which is a continuation-in-part of Application 07/425,224, filed October 20, 1989, now U.S. 5,013,556, patented May 7, 1991, with a different inventive entity. It appears that the applicants' references to Application 07/642,231, filed January 16, 1991, and claim for priority under 35 U.S.C. § 120, based on and stemming from said application, are incorrect. On the other hand, we note that Application 07/642,321, filed January 15, 1991, issued as U.S. 5,213,804 on May 25, 1993, to the same inventive entity as U.S. 5,013,556, patented May 7, 1991, and that the portion of the term of U.S. 5,213,804 subsequent to May 7, 2008, has been disclaimed.

Appeal No. 95-4004
Application 07/858,171

GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

This is an appeal from an examiner's rejection of Claims 1 and 4-7, all claims pending in this application. Claims 1 and 4-7 stand finally rejected under 35 U.S.C. § 103 as unpatentable over the teaching of Popescu et al. (Popescu), U.S. 4,981,692, patented January 1, 1991 (prior art under 35 U.S.C. § 102(e) based on its August 18, 1987, filing date), in view of the teachings of Radhakrishnan, U.S. 4,906,476, patented March 6, 1990 (prior art under 35 U.S.C. § 102(e) based on its December 14, 1988, filing date), and McGregor et al. (McGregor), U.S. 5,079,234, patented January 7, 1992 (prior art under 35 U.S.C. § 102(e) based on its March 23, 1989, filing date). All of the claims "stand or fall together" (Appeal Brief, page 3; Examiner's Answer, page 2).

Representative Claim 1 reads:

1. A method of treating a systemic infection which is localized at a site other than the fixed macrophages residing in the liver or the spleen, comprising

administering to the subject, by intravenous injection, a composition of liposomes (i) composed of vesicle-forming lipids, including 1-35 mole percent of a diacyl-chain amphipathic vesicle-forming lipid derivatized with polyethylene glycol having a molecular weight between about 350 and 5,000 daltons (ii) having a selected mean particle diameter in the size range between about 0.07-0.20 microns, and (iii) containing in liposome-entrapped form, a therapeutic compound effective against the source of the infection, and

Appeal No. 95-4004
Application 07/858,171

by said injecting, achieving at least about a ten-fold increase in the concentration of liposomes in the infected tissue over that achievable by the [sic] such liposomes in the absence of the amphipathic vesicle-forming lipid derivatized with said polyethylene glycol.

Having meticulously reviewed the specification, the claims, the prior art cited against the claimed invention, the Appeal Brief, and the Examiner's Answer, we find that the examiner has not satisfied his burden to establish a prima facie case of unpatentability of the claimed subject matter under 35 U.S.C. § 103 in view of the combined teachings of Popescu, Radhakrishnan, and McGregor. We find that no single prior art reference cited against the subject matter claimed describes the "diacyl-chain amphipathic vesicle-forming lipid derivatized with polyethylene glycol having a molecular weight between about 350 and 5,000 daltons" which is a required component of the vesicle forming lipids which comprise the liposome composition administered by intravenous injection in accordance with the method of Claim 1. Moreover, the prior art considered as a whole would not have reasonably led persons having ordinary skill in the art to make and use the vesicle-forming lipids which comprise that liposome composition to administer a therapeutic compound effective against a source of infection by intravenous injection as per the method of Claim 1.

Appeal No. 95-4004
Application 07/858,171

The examiner relies on Radhakrishnan and McGregor as support for the following statement (Examiner's Answer, page 3):

The size and weight of liposomes are within the capability of one of ordinary skill in the art to attain, if desiring to achieve particular dosage and/or organ targets. However, Radhakrishnan uses liposomes to deliver drugs of liposomal size 0.04-5 microns to lung (column 7), while McGregor specifies 1000-5000 dalton polymer size to provide biocompatibility (column 3, lines 28-30). Thus, it would be obvious to one of ordinary skill in the art of Liposome entrapped drug administration to provide the gentamicin antibiotic to treat Klebsiella infections of the lung, as included in the disease conditions of Popescu treatments, modified to provide increased safety and efficacy as taught by Radhakrishnan and McGregor.

We find, however, no teaching or suggestion in either Radhakrishnan or McGregor to use a "diacyl-chain amphipathic vesicle-forming lipid derivatized with polyethylene glycol having a molecular weight between about 350 and 5,000 daltons" (emphasis added) in the method of appellants' Claim 1 or for any other purpose. Moreover, the examiner's findings that Popescu describes and reasonably suggests a polyethylene glycol derivatized diacyl-chain amphipathic vesicle-forming lipid (Examiner's Answer, page 3) are clearly erroneous.

In its most relevant part, Popescu teaches (Popescu, column 3, line 64, to column 4, line 12):

The lipids which can be used in the liposome formulations of the present invention are the phospholipids such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylglycerol (PG), phosphatidic acid (PA), phosphatidylinositol (PI),

Appeal No. 95-4004
Application 07/858,171

sphingomyelin (SPM), and the like, alone or in combination. The phospholipids can be synthetic or derived from natural sources such as egg or soy. Useful synthetic phospholipids are dymyristoylphosphatidylcholine [sic](DMPC) and dimyristoylphosphatidylglycerol (DMPG). The liposomes can also contain other steroid components such as polyethylene glycol derivatives of cholesterol (PEG-cholesterols), coprostanol, cholestanol, or cholestane, and combinations of PC and cholesterol. They may also contain organic acid derivatives of sterols such as cholesterol hemisuccinate (CHS), and the like.

While Popescu describes "polyethylene glycol derivatives of cholesterol (PEG-cholesterols), coprostanol, cholestanol, or cholestane, and combinations of PC and cholesterol" (Popescu, column 4, lines 7-9), Popescu nowhere teaches or reasonably suggests the use of diacyl-chain amphipathic vesicle-forming lipids derivatized with polyethylene glycol as per Claim 1 of this appeal. The examiner finds that "PEG-cholesterolos [sic, cholesterols]" are part of "the instant invention (page 13, lines 19-26)" (Examiner's Answer, page 3). We hold that a finding that PEG-cholesterol is a "diacyl-chain amphipathic vesicle-forming lipid derivatized with polyethylene glycol" is clearly erroneous. We hold that PEG-cholesterols are not within the scope of the method appellants claim.

The examiner's reference to page 13, lines 19-26, of appellants' specification does not support the final rejection. The specification teaches (Specification, page 13, lines 16-31):

The vesicle-forming lipid is preferably one having two hydrocarbon chains, typically acyl chains, and a polar

Appeal No. 95-4004
Application 07/858,171

head group. Included in this class are the phospholipids such as phosphatidylcholine (PC), PE, phosphatidic acid (PA), phosphatidylinositol (PI), and sphingomyelin (SM), where the two hydrocarbon chains are typically between about 14-22 carbon atoms in length, and have varying degrees of unsaturation. Also included in this class are the glycolipids, such as cerebrosides and gangliosides.

Another vesicle-forming lipid which may be employed is cholesterol and related sterols. In general, cholesterol may be less tightly anchored to a lipid bilayer membrane, particularly when derivatized with a high molecular weight polymers [sic], such as polyalkylether, and therefore be less effective in promoting liposome evasion of the RES in the bloodstream.

The specification's teaching that cholesterol and related sterols derivatized with polyalkylether are suitable as vesicle-forming lipids for inclusion in liposome compositions containing therapeutic compounds for use in treating systemic infection localized at a site by intravenous injection is not a teaching or even a suggestion of the method of the claims on appeal. In short, the examiner clearly erred in finding that cholesterol and related sterols derivatized with polyalkylether are diacyl-chain amphipathic vesicle-forming lipids derivatized with polyethylene glycol having a molecular weight between about 350 and 5,000 daltons. Therefore, we must reverse the examiner's holding that Claims 1 and 4-7 on appeal are unpatentable under 35 U.S.C. § 103 over the teaching of Popescu in view of the teachings of Radhakrishnan and McGregor.

Other Issues

Appeal No. 95-4004
Application 07/858,171

We bring to the examiner's attention Woodle et al. (Woodle), U.S. 5,013,556, which issued May 7, 1991, from Application 07/425,224, filed October 20, 1989, and Martin et al. (Martin), U.S. 5,213,804, which issued May 25, 1993, from Application 07/642,321, filed January 15, 1991. The inventors of both patents are Martin C. Woodle, Francis J. Martin, Annie Yau-Young, and Carl T. Redemann. Copies of both patents are being mailed with this decision.

We remand this application to the examiner for consideration of the patentability of the subject matter claimed in this application in light of the subject matter disclosed and/or claimed in Woodle and Martin. The examiner should consider and determine the following:

(1) Whether applicants' claim for priority under 35 U.S.C. § 120 in this application is incorrect. This application and Application 07/642,231, filed January 16, 1991, do not have the same inventive entity, do not appear to be commonly assigned, and do not appear to be directed to either common or even similar inventions.

(2) Whether the full scope of the subject matter of the claims on appeal is entitled to the benefit of any one or both of the filing dates of Application 07/642,321, filed January 15, 1991, and Application 07/425,224, filed October 20, 1989.

Appeal No. 95-4004
Application 07/858,171

(3) Whether Woodle is prior art under 35 U.S.C. § 102(a) and/or § 102(e).

(4) Whether Woodle's Claims 22-27 are prior art under 35 U.S.C. § 102(f) or § 102(g).

(5) Whether Martin is prior art under 35 U.S.C. § 102(e).

(6) Whether Martin's Claims 11-14 are prior art under 35 U.S.C. § 102(f) or § 102(g).

(7) Whether the examiner is barred under 35 U.S.C. § 121 from rejecting the claims of this application for obviousness-type double patenting of Claims 22-27 of Woodle.

(8) Whether the examiner is barred under 35 U.S.C. § 121 from rejecting the claims of this application for obviousness-type double patenting of Claims 11-14 of Martin.

(9) Whether the claims of this application should be rejected for obviousness-type double patenting of Claims 22-27 of Woodle.

(10) Whether the claims of this application should be rejected for obviousness-type double patenting of Claims 11-14 of Martin.

We remand this application to the examiner to consider and resolve the questions raised in paragraphs (1) to (10) above. Without full consideration and resolution of these questions, we fail to see how the examiner can possibly determine the scope and

Appeal No. 95-4004
Application 07/858,171

content of the prior art, consider the state of and knowledge in the art at the time the invention was filed, and adequately determine the patentability of the claimed subject matter, i.e., examine the case.

This application, by virtue of its "special" status, requires an immediate action. Manual of Patent Examining Procedures § 708.01(d)(6th ed., rev. 3, July 1997). It is important that the Board be informed promptly of any action affecting the appeal in this case.

REVERSED; REMANDED

Sherman D. Winters)	
Administrative Patent Judge)	
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Richard E. Schafer)	BOARD OF PATENT
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Appeal No. 95-4004
Application 07/858,171